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Ulrich	
Application Number: 07/975,750	Filed: 11/13/92
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(12) **United States Patent**
Ullrich et al.

(10) **Patent No.: US 6,177,401 B1**
(45) **Date of Patent: Jan. 23, 2001**

(54) **USE OF ORGANIC COMPOUNDS FOR THE INHIBITION OF FLK-1 MEDIATED VASCULOGENESIS AND ANGIOGENESIS**

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(*) Notice: Under 35 U.S.C. 154(b), the term of this patent shall be extended for 0 days.

(21) Appl. No.: **08/193,829**

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Related U.S. Application Data

(63) Continuation-in-part of application No. 08/038,596, filed on Mar. 26, 1993, now abandoned, which is a continuation-in-part of application No. 07/975,750, filed on Nov. 13, 1992, now abandoned.

(51) **Int. Cl.**[7] **A61K 31/00**

(52) **U.S. Cl.** **514/1**; 435/7.2; 436/501; 530/350; 530/399

(58) **Field of Search** 536/23.5; 435/69.1, 435/172.1, 240.2, 252.3, 320.1, 325, 361, 7.2; 424/93.2; 514/44, 1; 935/32, 57, 70, 71; 436/501; 530/399, 350

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(57) **ABSTRACT**

The present invention relates to the use of proteins, peptides and organic molecules capable of modulating Flk-1 receptor signal transduction in order to inhibit or promote angiogenesis and vasculogenesis. The invention is based, in part, on the demonstration that Flk-1 tyrosine kinase receptor expression is associated with endothelial cells and the identification of vascular endothelial growth factor (VEGF) as the high affinity ligand of Flk-1. These results indicate a major role for Flk-1 in the signaling system during vasculogenesis and angiogenesis. Engineering of host cells that express Flk-1 and the uses of expressed Flk-1 to evaluate and screen for drugs and analogs of VEGF involved in Flk-1 modulation by either agonist or antagonist activities is described.

The invention also relates to the use of FLK-1 ligands, including VEGF agonists and antagonists, in the treatment of disorders, including cancer, by modulating vasculogenesis and angiogenesis.

16 Claims, 25 Drawing Sheets